UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,166	03/31/2004	Robert Karlsson	B 522	7149

22840 7590 05/12/2008

GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
05/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/815,166	KARLSSON ET AL.	
	Examiner	Art Unit	
	GAILENE R. GABEL	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *14-19 and 21-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 20* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Art Unit: 1641

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-13 and 20, without traverse, filed on January 29, 2007, is acknowledged and has been entered. Claims 14-19 and 21-34 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Currently, claims 1-34 are pending. Claims 1-13 and 20 are under examination.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

3. Claim 20 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 13. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-13 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in steps iv) and v) because it is unclear how any of the ligands can bind to intracellular analytes. It appears that a permeabilization step is needed to permeabilize the cells in the sample so as to allow ligands to penetrate the cell membrane and bind the intracellular analytes to which they are specific. It appears therefore, that claim 1 may be incomplete, at least with regards to detection of intracellular analytes.

Claim 1 step v) is further confusing because it is unclear how the binding agent comprising a specific binding pair is prevented from binding the ligands that have bound to cell-surface bound analyte or intracellularly bound analyte. Since the ligands have affinity for both cell-surface bound analyte or intracellularly bound analyte and also demonstrate specific binding to specific binding moiety present on the surface of the solid support, it is unclear how the specific binding moiety present on the solid surface can selectively or differentially bind unbound ligands over the bound ligands.

Claim 1 step vi) is also ambiguous because it is unclear how amount of binding of each ligand in step v) can be compared to the amount of binding of the same ligand in step iii). It appears that the amount of ligand used in step ii) should be predetermined and the same in concentration as that used in step v), in order to allow such comparison.

Claim 3 lacks clear antecedent basis in reciting, "cell fragments."

Claim 3 lacks clear antecedent basis in reciting, “cells and cell fragments are removed from the cell sample before [further] contacting… in step (v). Does Applicant intend to make reference to removing the cells having cell surface antigens that bound to ligands?

Claim 4 lacks clear antecedent basis in reciting, "and fragments."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-8, 10-13 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wahlstrom et al. (WO 96/38729) in view of Malmqvist et al. (US Patent 5,492,840).

Wahlstrom et al. teach a method of analyzing pathogenic cells (bacterial cells: Salmonella or Listeria) from a cell sample using modified inhibition type immunoassay method (p. 2, lines 11-29 and p. 3, lines 12-13). The method can also be used for application in detecting target cells expressing specific cell surface antigen or intracellular antigens present in blood sample (p. 3, lines 14-18). In practice, a predetermined amount of the cell sample is contacted with predetermined amount of antibodies (i.e. ligands) that specifically bind antigens on the cells, and then allowed to bind. The bound cells are separated from the mixture to obtain a cell free solution which contains unbound ligands. Separation or

removal of bound cells is performed by filtration or centrifugation method. The amount of unbound ligands or antibodies present in the solution is determined to provide detection of binding of ligands to the cells; thereby, indicating the presence of pathogenic or target cells present in the sample (p. 2, line 36 – p. 3, line 8 and p. 3, lines 24-26). Wahlstrom et al. specifically teach that the ligands are preferably added in predetermined excess amounts corresponding to the expected maximum amount of target cells, to leave unbound ligands in the reaction mixture (p. 3, lines 9-11). The amount of excess unbound ligand in the cell free solution is determined using a biosensor (solid phase) surface having immobilized thereto, binding partners or receptors that bind the unbound antibodies (see p. 3, lines 29-36 and p. 4, lines 18-23). The measurement is advantageously based on evanescent wave sensing, such as surface Plasmon resonance spectroscopy, evanescent wave ellipsometry, optical waveguide sensors, etc. (p. 4, line 36 – p. 5, line 28). The biosensor surface may be provided in a flow cell (see p. 4, lines 1-3).

Wahlstrom et al. differ from the instant invention in failing to teach that the solid phase surface (biosensor) having immobilized thereto, different binding agents at defined positions on the surface, is initially contacted with a set of different ligands or antibodies that specifically bind antigens present on the target cells and which also bind the receptors or binding agents present on the surface, so as to determine the amount of binding of each of the ligands to the solid support surface.

Malmqvist et al. disclose biosensors and methods for functionalizing sensing surfaces to be used in systems for simultaneously measuring the concentrations of a plurality of different biomolecules in a sample (Abstract). When measurements are carried out, the sensing surfaces are first functionlized with different binding agents or ligands for selective interaction with different desired biomolecules (c. 2, line 66 – c. 3, line 28 and c. 4, lines 17-30). Malmqvist et al. specifically teach that ligands employed may be [hetero]bifunctional or polyfunctional ligand molecules which contain anti-f function which is utilized for

immobilization into corresponding sensing surface and anti-f1-L1 to anti fn-Ln function for bioselective function for interaction and coupling to different ligands and different biomolecules present in the sample solution (c. 4, lines 31-46 and c. 6, line 54 – c. 7, line 32). Malmqvist et al. also provide that the sensing surface may be regenerated at two different levels, either for binding a new analyte or for refunctionalizing the surface with the same or other heterobifunctional ligand molecules (c. 8, lines 23-26).

One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Malmqvist in initially functionalizing the biosensor sensing surfaces with heterobifunctional ligands for binding and detection of the presence of analyte in a sample as in the method of Wahlstrom because Malmqvist specifically taught that his method allows for simultaneous measurement of several properties of one biomolecule, as well as simultaneous measurement of a plurality of biomolecules present in a sample.

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wahlstrom et al. (WO 96/38729) in view of Malmqvist et al. (US Patent 5,492,840) as applied to claims 1-8, 10-13 and 20 above, and further in view of Willmann et al. (US Patent 6,495,333).

Wahlstrom et al. and Malmqvist et al. are discussed supra. Wahlstrom et al. and Malmqvist et al. differ from the instant invention in failing to teach permeabilizing cell membranes so as to render cells permeable to ligands.

Willmann teach permeabilizing cell membranes of nucleated cells using permeabilizing solution so as to allow ligands (antibodies) to permeate the cell membrane and bind to intracellular antigens. See Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to permeabilize the cell membranes of cells in the method of Wahlstrom as modified by Malmqvist, using permeabilization solution as taught by Willmann for allowing ligands to permeate cell membrane and bind to intracellular antigens because Willmann specifically taught that cell membranes are impermeable to stains or antibody conjugated labels and that use of permeabilization solutions to render cell membranes permeable to stains is conventionally known in cell-based immunological assays, to permit contact and binding between labeled ligands and intracellular antigens specific thereto and to allow for detection and quantitation of intracellular proteins/analytes.

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GAILENE R. GABEL whose telephone number is (571)272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1641

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

May 8, 2008